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The Acute Toxicity of Phenol

Date of report 5-6-49

Tables of Protocols Attached

Carbide and Carbon Chemicals Corporation

Industrial Fellowship 274-12

Summary

The LD₅₀ for male 90 to 120 grams albino rats, fed a 5% solution of phenol by stomach tube and observed for 14 days, is 1.03 (0.94 to 1.12) gm./kg. Phenol would be classed as a moderately toxic compound by this route. It is about 1/3 as toxic as 3,5 Xylenol, 1/2 as toxic as m-cresol and 6 times as toxic as beta-naphthol based upon similar assays.

The LD₅₀ for rabbits by skin penetration is 0.63 (0.56 to 0.70) gm./kg. for a 10% aqueous dispersion applied for 24 hours under "Vinylite" sheeting. Phenol penetrates the skin rapidly and must be removed as soon as possible by washing with water if fatalities are to be avoided. It is more toxic when diluted in oil than in water presumably because of more rapid penetration through the skin.

Substantially saturated vapors prepared at room temperature and mist evolved by heating at 170° C. during aeration constitute a slight hazard by inhalation as rats tolerated 8 hour exposures to each with no deaths occurring in a 14 day observation period.

A 10% solution of phenol in acetone caused no reaction of greater severity than moderate erythema on the skin of the rabbit belly in the vesicant test. A 10% aqueous dispersion similarly applied resulted in marked erythema and edema.

Severe corneal damage is inflicted on the rabbit eye by 15% solutions in propylene glycol and to a lesser degree by 5% solutions. Its action on the eye may be compared to that of formaldehyde and di-n-hexyl amine.

Samples

Merck's Reagent Grade and Eimer and Amend C.P. Phenol were used for all of these tests with the exception of the studies on removal from rat skin. The sample used for the latter was labelled 100% phenol and was furnished by W. C. Rodgers of Bakelite Corp. on 4-21-43. This report is a recapitulation of the data previously reported with additional information on vapor inhalation and skin irritation.

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Single Oral Doses

The LD₅₀ for phenol, fed as 5% solution in water to male albino rats in the 90-120 gram weight range without previous starvation, is 1.02 (0.94 to 1.12) gm./kg. Thirty seconds after the administration of a dose by stomach tube violent tremors were apparent. Deaths ensued promptly after dosages in excess of the LD₅₀. Examination at autopsy revealed congested and hemorrhagic lungs, congested livers, pale kidneys bloated gastro-intestinal tracts, and occasional congestion of adrenal and pancreas. For comparison the following R.F. LD₅₀'s are quoted: 3,5-Xylenol 0.3 gm./kg., beta naphthol 5.9 gm./kg. and m-cresol 0.52 gm./kg.

In connection with an investigation of the effects of diluents and dispersants on the acute oral LD₅₀ determination 2 groups of 10 rats each were dosed at the LD₅₀ level reported above. The mortalities that resulted were 4 of 10 and 3 of 10 for a 5% aqueous solution and a 5% solution in 1% "Tergitol" respectively. Obviously, the comparison had to be made with a water soluble compound and phenol was chosen on that basis. The results incidentally confirmed the validity of the LD₅₀ calculation.

Skin Penetration

The LD₅₀ by skin penetration is 0.63 (0.56 to 0.70) ml./kg. for a 10% aqueous dispersion applied for 24 hours under impervious "Vinylite" sheeting to the entire clipped rabbit trunk. Tremors and prompt death followed the application to the skin. Erythema, edema, and sometimes necrosis were the resultant skin effects. The visceral organs were usually congested when examined at autopsy. It is notable that this compound penetrates the skin rapidly and is perhaps even more toxic by this route than by mouth. Other compounds that fall in the same toxicity grade are n-butyl amine, crotonic acid, ethylene diamine and formaldehyde. Report 12-34 of 3-3-49 contains the protocols of this test.

Inunction

A 4% solution of phenol in water applied by inunction killed 2 of 10 rabbits at 50 ml./kg. (2 gm./kg. of phenol) and the same concentration in a U.S.P. light mineral oil killed 4 of 4 rabbits at the same level and none of 5 at 25.2 ml./kg. Phenol therefore penetrates the skin more rapidly from oil than from water.

Removal of Phenol

Progress report 7-43, dated 5-31-44, summarizes the results of our studies on the removal of phenol and phenol plus substituted phenols from the skin of rats. The recommendation was made that water be used for first aid removal of phenols from the skin to prevent fatal results from absorption. The need for haste in removal was stressed.

The substituted phenols were less toxic quantitatively by skin absorption than phenol alone but they were more difficult to remove from the skin.

Inhalation

Substantially saturated phenol vapor at room temperature was generated by packing crystals of phenol and glass beads in layers separated by glass wool in a 100 ml. burette and aerating this column at 2.5 l./min. Rats tolerated an 8 hour exposure to the vapors and survived throughout a 14 day observation period.

Similarly 6 of 6 rats survived an 8 hour exposure to a mist produced by holding the compound in a bath at 170° C. while aeration was accomplished. Four of the 6 rats gained weight subnormally and 2 lost a few grams each. The hazard to life attendant upon inhalation of saturated vapor or mist for short intervals is considered to be slight, particularly so because the vapors are irritating to mucous membrane and thereby warn of their presence.

Irritation

In the rabbit belly vesicant test a 10% solution of phenol in acetone produced moderate erythema on 3 rabbits and marked injection on 2 others. A 10% aqueous dispersion produced reactions of greater severity; namely; marked erythema on 2 and edema on 3.

A 15% solution in propylene glycol caused severe damage to the cornea of rabbit eyes while 5% injured to a lesser extent. This relegates the compound to grade 8 in the 10 grade eye burn rating system which is represented by compounds such as formaldehyde, lactic acid, and di-n-hexylamine.

Charles P. Carpenter

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SENIOR INDUSTRIAL FELLOW

Typed: April 29, 1949

Table 12-70

PHENOL

Single Doses to Male Albino Rats by MouthFed by Stomach Tube as a Solution in Water, 1 ml. = 0.05 grams.

Rat No.	Date Dosed	Grams Wt.	Weight Change in 14 Days	Dosage; Grams per Kilo	Dose in Grams	Dose in ml. of Solution	Days to Death
41325	3-27-46	114	-	1.26	0.144	2.8	0
41326	"	110	-	1.26	0.139	2.8	0
41310	"	94	-	1.26	0.118	2.4	0
41312	"	100	-	1.26	0.126	2.5	0
41314	"	112	-	1.26	0.141	2.8	0
41317	"	104	-	1.26	0.131	2.6	0
41321	"	106	-	1.26	0.134	2.6	0
41319	"	95	-	1.26	0.120	2.2	0
41311	"	93	+ 49	1.26	0.117	2.3	-
41315	"	101	+ 78	1.26	0.127	2.5	-
41872	4-18-46	99	-	1.12	0.111	2.2	1
41881	"	92	-	1.12	0.103	2.0	1
41891	"	90	-	1.12	0.101	2.0	1
41898	"	90	-	1.12	0.101	2.0	0
41901	"	100	-	1.12	0.112	2.2	1
41911	"	99	-	1.12	0.111	2.2	0
41874	"	98	+ 91	1.12	0.110	2.2	-
41875	"	98	+ 78	1.12	0.110	2.2	-
41877	"	91	+ 74	1.12	0.102	2.0	-
41880	"	100	+ 73	1.12	0.112	2.2	-
40991	3-13-46	104	-	1.00	0.104	2.0	1
40994	"	102	-	1.00	0.102	2.0	1
40997	"	96	-	1.00	0.096	1.9	1
40998	"	95	-	1.00	0.095	1.9	1
41003	"	114	-	1.00	0.114	2.2	1
40984	"	98	+ 38	1.00	0.098	2.0	-
40989	"	111	+ 31	1.00	0.111	2.2	-
40993	"	110	+ 83	1.00	0.110	2.2	-
40999	"	100	+ 62	1.00	0.100	2.0	-
41001	"	103	+ 97	1.00	0.108	2.0	-
41850	4-18-46	97	-	0.89	0.0865	1.7	1
41831	"	90	+ 46	0.89	0.0800	1.6	-
41851	"	96	+ 68	0.89	0.0855	1.7	-
41852	"	94	+ 78	0.89	0.0836	1.6	-
41853	"	96	+ 57	0.89	0.0855	1.7	-
41860	"	100	+ 92	0.89	0.0890	1.8	-
41862	"	96	+ 70	0.89	0.0855	1.7	-
41863	"	93	+ 75	0.89	0.0830	1.6	-
41869	"	93	+ 8	0.89	0.0830	1.6	-
41839	"	93	+ 42	0.89	0.0830	1.6	-

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